REMARKS/ARGUMENTS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

Claims 13 and 14 have been amended so as to be placed in independent form. New claims 21 and 22 have been added. The newly added claims are fully supported by an enabling disclosure, including the claims as filed.

Claims 1-12 stand rejected under 35 USC 103 as allegedly being obvious over Ross et al in view of Shearer et al as evidenced by Rizzuto et al. Withdrawal of the rejection is submitted to be in order for the reasons that follow.

Ross et al relates to DNA vaccination with gp120-C3d fusion proteins. Ross et al report enhanced antibody titers and avidity maturation of antibodies to Env but poor titers of neutralizing antibody in vaccinated mice.

As the Examiner acknowledges, Ross et al is devoid of any teaching as regards a fusion protein comprising IgG Fc. The Examiner relies on Shearer et al to cure that deficiency.

Shearer et al relates to vertical transmission of HIV-1 and reports the results of a study designed to determine whether intravenously administered rCD4-IgG crosses the human placenta and whether it can be detected in human neonates. The study was not designed to address the question of efficacy of the rCD4-IgG fusion in blocking vertical HIV-1 transmission. The results appear to demonstrate that the bifunctional molecule can be transported across the placenta. No significant accumulation of rCD4-IgG was observed in an infant born to a mother who received multiple injections of rCD4-IgG.

In rejecting the claims as obvious, the Examiner contends that it would have been obvious to add the human IgG Fc component to the N- or C-terminus of the gp120-C3d fusion

protein of Ross et al for the purpose of increasing the serum half life of gp120-C3d and that there would have been a reasonable expectation of success because Shearer et al suggests that human IgG Fc prolongs the serum half life of the gp120 binding domain of CD4. Respectfully, these assertions do not constitute the type of reasoning required to support the contention that the combination of references would have led an artisan to the claimed invention.

Rejections under 35 USC 103 must rest on a factual basis with the facts being interpreted without hindsight reconstruction of the invention from the cited art (see *In re Warner*, 379 F2d 1011, 1017 (CCPA 1967), *cert denied* 389 U.S. 1057 (1968)). The Examiner's basis for rejection here falls short of identifying a rationale that would have led one skilled in the art to combine features from each of the references in a way that would have resulted in the claimed product (see *KSR Int'l Co. v. Teleflex, Inc.*, 127 S.Ct. 1727, 1741 (2007).)

Stated otherwise, nothing in the references upon which the Examiner relies would have suggested their combination. Indeed, the Examiner does not contend otherwise. Rather, the Examiner merely points out that Shearer et al suggests the use of IgG Fc to prolong the serum have life of the gp120 binding domain of CD4. Nothing in Ross et al and/or Shearer et al would have suggested a fusion protein comprising IgG Fc, gp120 and C3d, nor would the references have provided any basis for a reasonable expectation of generating a successful product.

In summary, it is only with the present invention in mind that one would have been motivated to combine the teachings of Ross et al and Shearer et al. It is now well established that such hindsight-based reasoning is improper and reconsideration is requested.

Claims 13, 14, 16 and 17 stand rejected under 35 USC 103 as allegedly being obvious over Ross et al in view of Shearer et al and De Vico et al as evidenced by Rizzuto et al. Withdrawal of the rejection is in order for the reasons that follow.

Claim 13 relates to a complex comprising the fusion protein of claim 1 wherein the HIV envelope component thereof is activated so that intermediate conformations of conserved neutralization epitopes are exposed. Claim 14, from which 16 and 17 depend, also relates to a complex comprising the fusion protein of claim 1. In claim 14, the HIV envelope component is bound to a ligand that upregulates at least one of a CD4 binding site and a CCR5 binding site of the envelope.

Ross et al relates to DNA vaccination with a gp120-C3d fusion and Shearer et al relates to the use of rCD4-IgG as a drug in blocking vertical transmission of HIV-1. As pointed out above, it is only with the present invention in mind that these documents would have been combined.

The Examiner acknowledges that neither Ross et al nor Shearer et al teaches activation of HIV envelope as required in claim 13 or binding of a ligand to envelope as required in claim 14. The Examiner looks to De Vico et al to cure these failing.

De Vico et al relates to a gp120-CD4 complex and reports that "the covalently bonded CD4-gp120 complexes are useful for raising neutralizing antibodies against various isolates of HIV-1 and against HIV-2."

Nothing in De Vico et al would have motivated an artisan to combine the teachings thereof with those of Ross et al (relating to DNA vaccination) and Shearer et al (relating to a vertical transmission blocking agent). Further, nothing in the combination upon which the Examiner relies in rejecting claims 13, 14, 16 and 17 would have provided basis for expecting success if all of the components had been assembled as claimed. Indeed, the Examiner does not indicate otherwise but, rather, the Examiner comments only on the combination of Shearer et al and Ross et al and, separately, on the combination of Ross et al and De Vico et al.

Reconsideration is requested.

Claims 13-15 stand rejected under 35 USC 103 as allegedly being obvious over Ross et al in view of Shearer et al and Wyatt et al. Withdrawal of the rejection is submitted to be in order for the reasons that follow.

The failings of Ross et al and Shearer et al are detailed above.

The Examiner acknowledges that neither Ross et al nor Shearer et al teaches a ligand-bound HIV Env. The Examiner looks to Wyatt et al to cure that failing.

Wyatt et al relates to a complex comprising HIV gp120 bound to a monoclonal antibody.

Nothing in Wyatt et al would have motivated an artisan to combine the teachings thereof with those of Ross et al (relating to DNA vaccination) and Shearer et al (relating to a vertical transmission blocking agent). Further, nothing in the combination upon which the Examiner relies in rejecting claims 13-15 would have provided basis for expecting success if all of the components had been assembled as claimed. Indeed, the Examiner does not indicate otherwise but, rather, the Examiner comments only on the combination of Shearer et al and Ross et al and, separately, the combination of Ross et al and Wyatt et al.

Reconsideration is requested.

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____
Mary J. Wilson
Reg. No. 32,955

MJW:tat
901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100